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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/048,072	01/25/2002	Genoveffa Franchini	15280-4003US	1664

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EXAMINER	
PARKIN, JEFFREY S	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 12/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/048,072	FRANCHINI ET AL.	
	Examiner	Art Unit	
	Jeffrey S. Parkin, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *03* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10 and 12-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 12-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Office Action

Status of the Claims

Acknowledgement is hereby made of receipt and entry of the communication filed 24 September, 2004. Claims 1-10 and 12-17 are currently under examination.

35 U.S.C. § 112, Second Paragraph

Claims 1-10 and 12-17 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Two separate requirements are set forth under this statute: (1) the claims must set forth the subject matter that applicants regard as their invention; and (2) the claims must particularly point out and distinctly define the metes and bounds of the subject matter that will be protected by the patent grant.

As previously set forth, the reference to an "efficient $CD8^+$ response" in an HIV-infected patient is vague and indefinite since it fails to clearly identify the salient characteristics of the CTL response. The claims fail to set forth the specificity and avidity of the $CD8^+$ response. The claims also fail to identify which populations of $CD8^+$ cells are being "activated" by the claimed methodology (i.e., CTL memory, effector, precursor). The claims fail to specify suitable administration parameters such as the target tissue (i.e., oral, mucosal, muscular), formulation, and vaccination regimens that lead to the desired response.

The reference to administration of a recombinant virus in claims 5-8 is also confusing since the claims are directed

toward the administration of a nucleic acid vaccine, not an attenuated virus. Applicants traverse and submit that the claim language is clear and definite in view of the specification. This argument is not deemed to be persuasive for the reasons set forth above. Applicants have failed to amend the claim language to address any of these deficiencies.

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Claims 1-10 and 12-17 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are broadly directed toward the administration of a human HIV CTL nucleic acid-based vaccine encoding different HIV structural immunogens. The legal considerations that govern enablement determinations pertaining to undue experimentation have been clearly set forth. *Enzo Biochem, Inc.*, 52 U.S.P.Q.2d 1129 (C.A.F.C. 1999). *In re Wands*, 8 U.S.P.Q.2d 1400 (C.A.F.C. 1988). *Ex parte Forman* 230 U.S.P.Q. 546 (PTO Bd. Pat. App. Int., 1986). The courts concluded that several factual inquiries should be considered when making such assessments including the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working

examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims. *In re Rainer*, 52 C.C.P.A. 1593, 347 F.2d 574, 146 U.S.P.Q. 218 (1965). The disclosure fails to provide adequate guidance pertaining to a number of these considerations as follows:

1) The disclosure fails to provide any guidance pertaining to the correlates of human protection. To date, it is not clear what type of immune response is required to provide a therapeutic benefit. What is the specificity of titer of the immune response required to provide an salubrious outcome? The disclosure is silent concerning this critical area.

2) HIV vaccines frequently fail because of the quasispecies nature of HIV infection. The plasticity of the HIV-1 genome and its contribution to immune escape are salient factors that have prevented the development of an effective vaccine. The disclosure fails to provide any data addressing this concern.

3) The disclosure fails to provide sufficient guidance pertaining to the most appropriate methods for presenting viral antigens to the immune system. The claims require a nucleic acid-based approach, however, there is nothing to suggest that this is the most efficient means for optimizing MHC Class I-dependent antigen uptake, processing, compartmentalization, and presentation.

4) The disclosure fails to provide sufficient guidance pertaining to those immunogens that are capable of conferring protection. Which CTL epitopes are capable of stimulating a strong and long-lasting immune response?

5) The disclosure fails to provide any guidance pertaining to the ability of any given mono-MHC-specific CTL vaccine to confer protection against an outbred population containing disparate MHC Class I alleles. Thus, it is not clear if the claimed invention would provide protection in a heterogenous population.

6) The disclosure fails to provide any working embodiments. The only human example is purely prophetic and fails to set forth any meaningful data. Some data was provided from the macaque model, however, this model is not an art-recognized model for vaccine development. Although animal models, such as the macaque system, are capable of providing important information pertaining to the understanding of pathogenesis and immunity, the results from such studies can not be directly extrapolated to a clinical setting due to the structural differences between SIV and HIV.

7) The disclosure fails to provide any guidance pertaining to the multiple polypmorphisms that exist within the peptide processing complex, or low molecular mass polypeptide complex (LMP), and the transport apparatus (i.e. the transporter associated with antigen processing (TAP) protein). This results in the presentation of different epitopes derived from the same antigen to the T-cell repertoire in different individuals.

8) The disclosure fails to provide any guidance pertaining to the development of a persistent and protective HIV-1-specific immune response. It is not readily apparent if the recited CTL vaccine will generate an HIV-1-specific immune response of sufficient magnitude and duration that long-lasting salubrious effects against HIV-1 infection and the development of AIDS would be provided. The specification does not provide any guidance pertaining to the prevention of HIV-1 transmission following the administration of said vaccine. As described in the preceding paragraph, there is no indication that an HIV-1-specific immune response has been generated and that such a response, if generated, would be protective following exposure to HIV-1.

9) The state-of-the-art vis-à-vis HIV CTL vaccine development is one of unpredictability (Haynes *et al.*, 1996; Burton and Moore, 1998; Moore and Burton, 1999; Desrosiers, R., 2004). To date, there is not one single effective HIV vaccine on the market.

Several clinical trials have been conducted but in every situation, the immunogen failed to induce a long-lasting and high-titer immune response.

Accordingly, when all the aforementioned factors are considered *in toto*, it would clearly require undue experimentation from the skilled artisan to practice the claimed invention.

Correspondence

Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (571) 272-0908. The examiner can normally be reached Monday through Thursday from 10:30 AM to 9:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, James C. Housel, can be reached at (571) 272-0902. Direct general status inquiries to the Technology Center 1600 receptionist at (571) 272-1600. Formal communications may be submitted through the official facsimile number which is (703) 872-9306. Hand-carried formal communications should be directed toward the customer window located in Crystal Plaza Two, 2011 South Clark Place, Arlington, VA. Applicants are directed toward the O.G. Notice for further guidance. 1280 O.G. 681. Informal communications may be submitted to the Examiner's RightFAX account at (571) 273-0908.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on

access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,

Jeffrey S. Parkin, Ph.D.
Patent Examiner
Art Unit 1648

12 December, 2004